201-16622A

HIGH PRODUCTION VOLUME (HPV) CHEMICAL CHALLENGE PROGRAM

Final Submission

For

Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide

CAS No. 80-51-3

Submitted to the US EPA

by

Chemtura (formerly Crompton) Corporation

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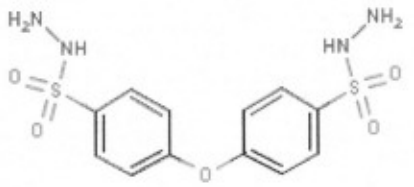
Test Plan for 4, 4'-oxydibenzenesulfonohydrazide

1. General Information

1.1 CAS Number: 80-51-3

1.2 Molecular Weight: 358.39

1.3 Structure and formula: $C_{12}H_{14}N_4O_5S_2$



1.4 Introduction

Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide is used as a chemical blowing agent in the manufacture of foam robber and plastic products.

2. Review of Existing Data

Crompton Corporation has undertaken a comprehensive evaluation of all relevant data on the SIDS endpoints of concern for Celogen OT. The availability of the data on the specific SIDS endpoints is summarized in Table 1.

Table 1: Available adequate data on Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide

CAS NO. 80-51-3	Information Available?	GLP	OECD Study?	Other Study?	Estimation Method?	Acceptable?	SIDS Testing Required?
	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
Physicochemical							
Melting Point	Y	N				Y	N
Boiling Point	Y	N				Y	N
Vapour Pressure	Y	N			Y	Y	N
Water Solubility	Y	Y	Y			Y	N
Partition Coefficient (Kow)	Y	N			Y	Y	N
Environmental Fate							
Biodegradation	Y	Y	Y			Y	N
Hydrolysis	N						N
Photodegradation	Y				Y	Y	N
Transport and Distribution between Environmental Compartments	Y				Y	Y	N
Ecotoxicology							
Acute Fish	Y	Y				Y	N
Acute Daphnia	Y	Y				Y	N
Acute Algae	Y	Y				Y	N
Toxicology							
Acute Oral	Y	N		Y		Y	N
Repeat Dose toxicity	Y	Y	Y			Y	N
Genetic toxicity – Gene mutation	Y	Y	Y			Y	N
Genetic toxicity – Chromosome Aberration	Y	Y	Y			Y	N
Reproductive toxicity	Y	Y	Y				N
Developmental toxicity/teratogenicity	Y	Y	Y				N

A. Evaluation of Physiochemical Data

1. Melting Point

It is reported in a peer-reviewed publication that Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide begins to decompose at 150-160°C prior to melting.

2. Boiling Point

The boiling point of Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide cannot be measured as the substance decomposes prior to melting.

3. Vapour Pressure

The vapour pressure was calculated to be 8.9x10-12 hPa at 25°C using MPBPWIN v1.40.

4. Water Solubility

The water solubility of Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide is 0.10996 mg/l at 20 °C (OECD TG 105).

5. Partition Coefficient

The log Pow of Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide was estimated to be 0.08 using KOWWIN vl.66.

Summary of Physicochemical Properties Testing: Existing data for melting point, boiling point, vapor pressure, water solubility and partition coefficient are considered to fill these endpoints adequately.

B. Evaluation of Environmental Fate Data

1. Biodegradation

Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide was not readily biodegradable in an OECD TG 301 B biodegradability study.

2. Hydrolysis

There are no hydrolysable groups in the chemical structure, and the substance is therefore predicted to be hydrolytically stable.

3. Photodegradation

The potential for photodegradation of Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide has been estimated using AOPWIN v1.90, and indicated atmospheric oxidation via OH radicals reaction with a half-life of 61 hours.

4. Transport and Distribution between Environmental Compartments

An Epiwin Level III Fugacity Model calculation has been conducted for Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide and indicates even distribution between soil and water for emissions of 1000 kg/hr

simultaneously to air, water and soil compartments.

Summary of Environmental Fate Testing: Existing data for photodegradation, biodegradation and transport and distribution between environmental compartments are considered to fill these endpoints adequately.

C. Evaluation of Existing Ecotoxicity Data and Proposed Testing

1. Acute Toxicity to Fish

Groups of fish (Cyprinus carpio) were exposed to concentrations of 2, 4, 8, 16 and 32 mg/L for 96 hours following OECD TG 203. Measured concentrations were .82, 1.54, 3.34, 6.35 and 12.89mg/L; the percent mortalities at the end of the test were 0, 10, 30, 60 and 100, respectively. The EC50 was 4.58 mg/L.

2. Acute Toxicity to Algae

The test item was tested at concentrations of .1, .35, 1.23, 4.29 and 15.01 mg/L along with a negative control, a vehicle control and a positive control. The cell growth was measured at 24, 48, and 72 hours after initiation of the test. The study followed OECD TG 201. The 72 hour values were:

EbC50 = 0.67 mg/L

ErC50 = 2.34 mg/L

NOEC = .1 mg/L

LOEC = .35 mg/L

3. Acute Toxicity to Daphnia

The Daphnia, less than 24 hours old, were exposed to concentrations of 4, 6.4, 10.24, 16.38 and 26.21 mg/L. The study followed OECD TG 202. At 24 hours the percent immobilization was 0, 0, 15, 40, and 60 (respective to the test item concentrations). At 48 hours the values for percent immobilization were 0, 25, 40, 65, and 100. The EC50 was 11.1 mg/L.

Acute toxicity to Fish, Daphnia and Algae studies are considered to fill these endpoints adequately.

D. Evaluation of Human Health Effects Data

1. Acute Oral Toxicity

The acute oral toxicity has been determined to be > 5200 mg/kg b.w. The acute dermal toxicity has been determined to be > 200 mg/kg b.w. (FIFRA Section 162.8(c)). When administered by interperitoneal injection, a LD50 >5000 mg/kg b.w. was observed. No further data on purity of the test material, tested doses, and systemic toxicity in target organs by dose and sex are available.

2. Skin Irritation

This non-SIDS endpoint has been evaluated for Celogen OT. Slight irritation occurred in rabbits treated with an aqueous extract of the chemical.

3. Repeat Dose Toxicity

In an OECD TG 422 study, the test item was mixed in the experimental food at the concentrations of 100, 500 and 1500 ppm and fed to three groups of rats i.e., low, mid and high dose/high dose recovery groups, respectively. Concurrent control group and a control recovery group of rats received experimental food without the test item. The main groups i.e., consisted of 10 male and 10 female rats per group and recovery groups consisted of 5 male and 5 female rats per group. There were no changes of clear toxicological significance noted among animals that received a dietary concentration of 500 ppm, this level is considered to be the NOAEL of 4,4'-oxybis(benzenesulfonylhydrazide) in rats, which is equivalent to 35.1 and 41.4 mg/kg bw/day for male and female rats, respectively.

Two repeat dose toxicity studies are reported in the literature. In the first of these a NOEL of 1 mg/kg bw/day (90 day, oral feed, rat) was reported. In the second study a LOAEL of 36 mg/kg/day (4 month, gavage, rat) was reported.

4. Genotoxicity

The substance was positive in a bacterial reverse mutation assay conducted following OECD TG 471. The substance was mutagenic in the Ames test (S. typhimurium) with and without metabolic activation and also with one strain of Escherichia coli with metabolic activation. With other strains of E. coli, the substance was found to be non-mutagenic with or without metabolic activation.

There was no evidence of induction of chromosome aberrations in any of the trials with the test item in a study following OECD TG 473. The substance gave negative results in a chromosome aberration study using human lymphocytes. It also gave negative results in a micronucleus assay and UDS assay.

5. Reproductive and Developmental Toxicity
In an OECD TG 422 study, the test item was mixed in the experimental food at

the concentrations of 100, 500 and 1500 ppm and fed to three groups of rats i.e., low, mid and high dose/high dose recovery groups, respectively. Concurrent control group and a control recovery group of rats received experimental food without the test item. The main groups i.e., consisted of 10 male and 10 female rats per group and recovery groups consisted of 5 male and 5 female rats per group. There were no changes of clear toxicological significance noted among animals that received a dietary concentration of 500 ppm, this level is considered to be the NOAEL of 4,4'-oxybis(benzenesulfonylhydrazide) for reproductive and developmental effects in rats, which is equivalent to 35.1 and 41.4 mg/kg bw/day for male and female rats, respectively.

Summary of Human Health Effects Testing: All endpoints are considered to have been filled adequately.

3. Evaluation of Data for Quality and Acceptability

The collected data were reviewed for quality and acceptability following the general US EPA guidance [2] and the systematic approach described by Klimisch et al [3]. These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. This scoring system was only applied to ecotoxicology and human health endpoint studies per EPA recommendation [4]. The codification described by Klimisch specifies four categories of reliability for describing data adequacy. These are:

(1) Reliable without restriction: Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.

(2) Reliable with Restrictions: Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.

(3) Not Reliable: Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.

(4) Not Assignable: Includes studies or data in which insufficient detail is reported to assign a rating, e.g. listed in abstracts or secondary literature.

4. Conclusion

Chemtura Corporation has met its commitment for the sponsorship of Benzenesulfonic acid, 4, 4'-oxybis-, dihydrazide (Celogen OT) under the US EPA HPV Challenge Program.

5. References

[1] US EPA, EPI Suite Software, 2000

[2] USEPA (1998). Guidance for Meeting the SIDS Requirements (The SIDS Guide). Guidance for the HPV Challenge Program. Dated 1 l/2/98.

[3] Klimisch, H.-J., et al (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. Regul. Toxicol. Pharmacol. 25: l-5

[4] USEPA (1999). Determining the Adequacy of Existing Data. Guidance for the HPV Challenge Program. Draft dated 2/10/99.